PATENT COOPERATION TREATY

	From the INTERNATIONAL BUREAU
PCT	То:
NOTIFICATION OF ELECTION (PCT Rule 61.2)	Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ÉTATS-UNIS D'AMÉRIQUE
Date of mailing: 10 September 1999 (10.09.99)	in its capacity as elected Office
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International filing date: 05 March 1999 (05.03.99)	Priority date: 06 March 1998 (06.03.98)
Applicant: SUMIDA, Shuji et al	
in a notice effecting later election filed with the Inte	
made before the expiration of 19 months from the priority Rule 32.2(b).	y date or, where Rule 32 applies, within the time limit under
The International Bureau of WIPO 34, chemin des Colombettes	Authorized officer:
1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	J. Zahra Telephone No.: (41-22) 338.83.38

PCT

国際事務局 特許協力条約に基づいて公開された国際出願

世界知的所有権機関



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PCT/JP99/01080

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(81) 指定国 AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, 欧州特許 (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI特許 (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG), ARIPO特許 (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), ユーラシア特許 (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM)

添付公開書類

国際調査報告書

(54)Title: PROTEIN-FREE PREPARATIONS

(54)発明の名称 蛋白非添加製剤

(57) Abstract
Stable preparations containing granulocyte colony stimulating factor which contain the granulocyte colony stimulating factor and 1 part by weight or less, per 1 part by weight of the granulocyte colony stimulating factor, of at least 1 pharmaceutically acceptable surfactant and have a pH value of 7 or lower.

Applicant's or agent's file reference

International application No.

YCT-395

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INTERNATIONAL PRELIMINARY EXAM

ONAL PRELIMINARY EXA	MIN	ATION REPORT	NTER 1600/29	R 1 2 2
(PCT Article 36 and Rule	70)		00/290(ZOOZ PET
		ionofTransmittalofInternat Report (Form PCT/IPEA/		inary
International filing date (day/month/y	rear)	Priority date (day/month	/year)	
05 March 1999 (05.03.99))	06 March 1998	(06.03.98)	
tional classification and IPC		<u> </u>		

	PC1/JP99/01080	05 March 19	999 (05.03.99)	06 March 1998 (06.03.98)
Interna	ational Patent Classification (IPC) or na A61K 38/17	ational classification a	and IPC	
A 12		·		
Applic	CHU	JGAI SEIYAKU	KABUSHIKI KAI	SHA
1.	This international preliminary exami and is transmitted to the applicant ac			national Preliminary Examining Authority
2.	This REPORT consists of a total of	5 sheet	s, including this cover s	sheet.
		this report and/or she	ets containing rectifica	on, claims and/or drawings which have been tions made before this Authority (see Rule
	These annexes consist of a tot	al of	sheets.	
3.	This report contains indications relat	ing to the following it	ems:	
	I Basis of the report			
	II Priority			
	III Non-establishment o	f opinion with regard	to novelty, inventive st	ep and industrial applicability
	IV Lack of unity of inve	ntion		
	V Reasoned statement citations and explana	under Article 35(2) w tions supporting such	ith regard to novelty, in statement	ventive step or industrial applicability;
	VI Certain documents ci	ted		
	VII Certain defects in the	international applica	tion	· ·
	VIII Certain observations	on the international a	pplication	•
Date o	of submission of the demand		Date of completion of	of this report
	05 March 1999 (05.03	.99)	30 Sep	ptember 1999 (30.09.1999)
Name	and mailing address of the IPEA/JP	,	Authorized officer	
	•			

Date of submission of the demand	Date of completion of this report
05 March 1999 (05.03.99)	30 September 1999 (30.09.1999)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP99/01080

I.	Basis	s of the report
1.	With	regard to the elements of the international application:*
	\boxtimes	the international application as originally filed
		the description:
		pages , as originally filed
		pages, filed with the demand
		pages, filed with the letter of
		the claims:
	_	pages, as originally filed
		pages, as amended (together with any statement under Article 19
		pages, filed with the demand
		pages, filed with the letter of
		the drawings:
		pages, as originally filed
		pages, filed with the demand
		pages, filed with the letter of
		the sequence listing part of the description:
	ш,	
		, as digitally filed
		pages, filed with the demand pages, filed with the letter of
2.	the ir	regard to the language, all the elements marked above were available or furnished to this Authority in the language in which international application was filed, unless otherwise indicated under this item. e elements were available or furnished to this Authority in the following language which is: the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/ or 55.3).
3.	With	regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international minary examination was carried out on the basis of the sequence listing: contained in the international application in written form.
	\Box	filed together with the international application in computer readable form.
		furnished subsequently to this Authority in written form.
		furnished subsequently to this Authority in computer readable form.
		The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
		The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
4.	\Box	The amendments have resulted in the cancellation of:
٠.		
		the description, pages
		the claims, Nos the drawings, sheets/fig
5.		This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**
	in thi	cement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to s report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 0.17).
**.	Any re	eplacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

'INTERNATIONAL PRELIMINARY EXAMINATION REPORT

mernational application No.
PCT/JP 99/01080

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
 citations and explanations supporting such statement

Statement			,
Novelty (N)	Claims	4,5	YES
· · · · · · · · · · · · · · · · · · ·	Claims	1-3, 6-12	NO
Inventive step (IS)	Claims	· · ·	YES
	Claims	1-12	NO
Industrial applicability (IA)	Claims	1-12	YES
	Claims		NO

2. Citations and explanations

• Claims 1-3 and 6-12

Document 1, Claim 7, discloses an aqueous pharmacological preparation which contains a therapeutically effective quantity of granulocyte colony stimulating factor and a quantity of surfactant no greater than the quantity of granulocyte colony stimulating factor employed, and which does not contain protein as a stabilizer. Examples 4, 5 and 7-9 further describe preparations which contain polysorbate(80) as a surfactant at more than 0.2 part by weight to 1 part by weight of granulocyte colony stimulating factor, and do not contain protein as a stabilizer.

Document 2, in Claims 10 which refers back to Claims 1, 2 and 8, discloses storage-ready pharmaceutical preparations containing granulocyte colony stimulating factor for use as a liquid injection or infusion, to which at least one preservative is added at a concentration of up to 2% during the production of the preparation, although this can be omitted if desired, with benzalkonium chloride, widely used as a surfactant, included as a possible preservative, wherein the pH of the preparation is approximately 2.0 to approximately 7.4. In Examples 6-9 it describes preparations which do not contain protein as

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a stabilizer, in which the ratio of recombinant human granulocyte stimulating factor and polysorbate(80) is 7:2.

Document 3, Claim 2, discloses freeze-dried preparations which further include a physiologically permissible surfactant at less than the quantity of granulocyte colony stimulating factor employed, or at most the same quantity; and Claim 11 indicates that the pH of pharmacological preparations in the form of aqueous solutions obtained by redissolving the freeze-dried preparations in Claim 2 is 6.5-8 or 3-5. Moreover, Example 10 describes a preparation in which Tween 80 and polysorbate(80) exceed 0.2 parts by weight to 1 part by weight of granulocyte colony stimulating factor and which do not contain protein as a stabilizer.

All of the preparations described in these examples are the same as the invention according to Claims 1-3, 6-8 and 12.

Therefore, Claims 1-3, 6-8 and 12 are not novel because they are disclosed in Documents 1 to 3.

• Claims 4 and 5

Documents 1 to 3 do not disclose the invention as described in Claims 4 and 5, wherein there is 0.4-0.8 parts by weight of surfactant to 1 part by weight of granulocyte colony stimulating factor.

However, the fact that this ratio of ingredients is suitable when it comes to producing preparations does not go beyond the conventional wisdom of a person skilled in the art. Therefore, given the disclosures in Documents 1 to 3, setting a suitable ratio of granulocyte colony stimulating factor and surfactant, and a suitable pH value, is not especially difficult for a person skilled in the art.

Therefore, Claims 4 and 5 do not involve an inventive step.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP 99/01080

Document 1 : JP, 8-505610, A

Document 2 : JP, 6-510031, A

Document 3 : JP, 8-504784, A

特 許 協 力 条 約

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出願人代理人

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PCT

(法施行規則第57条) [PCT規則71.1]

発送日

(日.月.年)

12.10.99

出願人又は代理人の書類記号

YCT-395

重要な通知

国際出願番号

PCT/JP99/01080

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(日.月.年) 05.03.99

優先日

(日.月.年) 06.03.98

出願人(氏名又は名称)

中外製薬株式会社

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名称及びあて名

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特 許 庁 長 官

4C 9736

電話番号 03-3581-1101 内線 3452

(添付用紙の注意書きを参照)

今後の手続きについては、国際予備審査報告の送付通知(様式PCT/

IPEA/416)を参照すること。

PCT

国際予備審査報告

(法第12条、法施行規則第56条) [PCT36条及びPCT規則70]

YCT-395

出願人又は代理人

の書類記号

国際出願番号 PCT/JP99/01080	国際出願日 (日.月.年) 05.	03.99	優先日 (日.月.年) 	06.03.98
国際特許分類 (IPC) Int.Cl A 6 1 I	38/17			
出願人(氏名又は名称) 中	外 製 薬 株	未 式 会	社	
1 国際予備審査機関が作成したこの	国際予備審査報告を法施		 C T 3 6 条)の規	 定に従い送付する。
2. この国際予備審査報告は、この表		•	ジからなる。	
□ この国際予備審査報告には、 査機関に対してした訂正を含 (PCT規則70.16及びPCT この附属掛類は、全部で	む明細書、請求の範囲及	び/又は図面も添(R)	基礎とされた及び すされている。	*/又はこの国際予備審
3. この国際予備審査報告は、次の内	容を含む。			
I X 国際予備審査報告の基礎				
Ⅱ [] 優先権 、	**************************************			
Ⅲ □⟨新規性、進歩性又は産業	終上の利用可能性について	ての国際予備審査報	告の不作成	
IV		•		
V X PCT35条(2)に規定 の文献及び説明	する新規性、進歩性又は	産業上の利用可能	生についての見解	よ、それを裏付けるため
VI ある種の引用文献				
VII 国際出願の不備				
VII 国際出願に対する意見				
· ·				

国際予備審査の請求書を受理した日 05.03.99	国際予備審査報告を作成した日 30.09.99	
名称及びあて先 日本国特許庁 (IPEA/JP)	特許庁審査官(権限のある職員)	4C 9736
郵便番号100-8915 東京都千代田区館が関三丁目4番3号	瀬下 浩一	
	電話番号 03-3581-1101 内	線 3452

I. 国際予備審査報告の基礎		
1. この国際予備審査報告は下記の出願書類に 応答するために提出された差し替え用紙は PCT規則70.16,70.17)	こ基づいて作成され は、この報告書には	れた。 (法第6条 (PCT14条) の規定に基づく命令において「出願時」とし、本報告書には添付しない。
X 出願時の国際出願書類		
明細書 第 明細書 第 明細書 第	ページ、 ページ、 ページ、	出願時に提出されたもの 国際予備審査の請求書と共に提出されたもの 付の書簡と共に提出されたもの
請求の範囲 第	項、 項、 項、 項、	出願時に提出されたもの PCT19条の規定に基づき補正されたもの 国際予備審査の請求郡と共に提出されたもの 付の書簡と共に提出されたもの
図面 第 図面 第 図面 第	ページ/図、 ページ/図、 ページ/図、	出願時に提出されたもの 国際予備審査の請求審と共に提出されたもの 一一一一一付の書簡と共に提出されたもの
回期細書の配列表の部分 第 明細書の配列表の部分 第 明細書の配列表の部分 第	ページ、 ページ、 ページ、	出願時に提出されたもの 国際予備審査の請求書と共に提出されたもの
上記の書類は、下記の言語である □ 国際調査のために提出されたPCT □ PCT規則48.3(b)にいう国際公開の □ 国際予備審査のために提出されたP	の言語	う翻訳文の言語
□ この国際出願に含まれる書面による □ この国際出願と共に提出されたフレ □ 出願後に、この国際予備審査(また □ 出願後に、この国際予備審査(また □ 出願後に提出した書面による配列表書の提出があった	配列表 シキシブルディスク は調査)機関に抵 は調査)機関に抵 な出願時における	
4. 補正により、下記の書類が削除された。 明細哲 第 請求の範囲 第 図面 図面の第	ページ 項 ペー	ジ / 図
5. □ この国際予備審査報告は、補充欄に示しれるので、その補正がされなかったもの記1. における判断の際に考慮しなけれ	のとして作成した。	が出願時における開示の範囲を越えてされたものと認めら 。(PCT規則70.2(c) この補正を含む差し替え用紙は上 告に添付する。)
•		

国際予備審査報告		国際出願番号	PCT/JP99/	01080
V. 新規性、進歩性又は産業上の利用可能性に 文献及び説明	ついての法第128	条 (PCT35	条(2)) に定める見解 	、それを裏付ける
1. 見解	•	,	, ·	
新規性(N)	請求の範囲 請求の範囲		4, 5 1-3, 6-12	有 無
進歩性(IS)	請求の範囲 請求の範囲		1-12	
産業上の利用可能性(IA)	請求の範囲 請求の範囲		1-12	有 無
				
2. 文献及び説明(PCT規則70.7)				
○請求の範囲1-3,6-12に 文献1の請求項7には、治療的 顆粒球コロニー刺激因子の量以下 パク質を含有しない水性薬理製剤 おいては界面活性剤としてのポリ 0.2重量部を越え、かつ安定化 ている。	に有効な量の の量の界面活 」が記載されて ソルベート80 、剤としてのタ	性剤を含有 いる。また が顆粒球コ ンパク質を	し、安定化剤で 、実施例4,5 ロニー刺激因子 含有しないもの	1,7-9に かい
くいる。 文献2の請求項1、2及び8を 田オスための顆粒球コロニー刺激	受ける請求項 大田子を含有す	〔10には、 る保存処理	注射又は注入浴 された医薬製剤	F液として使 引であって、

文献2の請求項1、2及び8を受ける請求項10には、注射又は注人裕液として使用するための顆粒球コロニー刺激因子を含有する保存処理された医薬製剤であって、該医薬製剤の製造中に少なくとも1種の保存剤を2%までの濃度で添加し、所望により除去してもよいものであり、保存剤として界面活性剤として広く用いられる塩化ベンザルコニウムを含み、pHが約2.0~約7.4であるものが記載されている。そして、実施例6-9には組換えヒト顆粒球コロニー刺激因子とポリソルベート80との比が7:2であって安定化剤としてのタンパク質を含有しない溶液が記載されている。

文献3の請求項2には、使用している顆粒球コロニー刺激因子の量より少ない又は最大でそれと同量である生理学的に寛容される界面活性剤を更に含む凍結乾燥製剤が記載されており、また請求項11には、請求項2に記載の凍結乾燥製剤の再溶解により得られる水溶薬理製剤のpH値が6.5~8又は3~5のものが記載されている。さらに実施例10には、界面活性剤としてTween 80及びポリソルベート80が顆粒球コロニー刺激因子に対して0.2重量部を越え、かつ安定化剤としてのタンパク質を含有しないものが記載されている。

- ないものが記載されている。 そして、これらの実施例に記載されているものは、いずれも本願の請求の範囲1-3、6-8及び12に係る発明とは同一である。

3、6~8及び12に保る光列とは同じてある。 従って、請求の範囲1-3、6-8及び12は文献1ないし3に記載されているか ら新規性を有さない。

○請求の範囲4,5について 文献1ないし3には、請求の範囲4及び5の発明である、界面活性剤が顆粒球コロー刺激因子に対して0.4~0.8重量部であるものが記載されていない。 しかしながら、製剤の製造に際し、その成分比などの値を適当な値とすることは当業者が通常認識する程度の事項であるにすぎないから、文献1ないし3の記載に基づき、顆粒球コロニー刺激因子と界面活性剤の比率及び製剤のpHの値を適宜設定することは、当業者にとって格別困難な事項であるとはいえない。 従って、請求の範囲4及び5は、進歩性を有さない。

国際予備審査報告

国際出願番号 PCT/JP99/01080

補充欄 (いずれかの欄の大きさが足りない場合に使用すること)

第 V 欄の続き

文献1:JP, 8-505610, A 文献2:JP, 6-510031, A 文献3:JP, 8-504784, A

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

SHAMOTO, Ichio Yuasa and Hara Section 206, New Ohtemachi Building 2-1. Ohtemachi 2-chome Chiyoda-ku Tokyo 100-0004 JAPON

Date of mailing (day/month/year) 30 April 1999 (30.04.99)	
Applicant's or agent's file reference YCT-395	IMPORTANT NOTIFICATION
International application No. PCT/JP99/01080	International filing date (day/month/year) 05 March 1999 (05.03.99)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 06 March 1998 (06.03.98)

CHUGAI SEIYAKU KABUSHIKI KAISHA et al

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date

Priority application No.

Country or regional Office or PCT receiving Office

Date of receipt of priority document

06 Marc 1998 (06.03.98)

10/54799

JP

26 Apri 1999 (26.04.99)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

Marc Salzman

Telephone No. (41-22) 338.83.38

Facsimile No. (41-22) 740.14.35

PATENT COOPERATION TREATY 09/622487

PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

SHAMOTO, Ichio Yuasa and Hara Section 206, New Ohtemachi Building 2-1, Ohtemachi 2-chome Chivoda-ku Tokyo 100-0004 **JAPON**

Date of mailing (day/month/year)

10 September 1999 (10.09.99)

Applicant's or agent's file reference

YCT-395

IMPORTANT NOTICE

International application No. PCT/JP99/01080

International filing date (day/month/year)

Priority date (day/month/year) 06 March 1998 (06.03.98)

05 March 1999 (05.03.99)

Applicant

CHUGAI SEIYAKU KABUSHIKI KAISHA et al

Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice: AU,CN,EP,IL,JP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CU,CZ,DE,DK,EA,EE,ES,FI,GB,GD,GE,GH,GM,HR,HU, ID,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,RO,RU,SD,

SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZW
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 10 September 1999 (10.09.99) under No. WO 99/44630

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

J. Zahra

Telephone No. (41-22) 338.83.38

Facsimile No. (41-22) 740.14.35

PATENT COOPERATION TREATY 09/622487

PCT

INFORMATION CONCERNING ELECTED OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

From the INTERNATIONAL BUREAU

SHAMOTO, Ichio Yuasa and Hara Section 206, New Ohtemachi Building 2-1, Ohtemachi 2-chome

Chiyoda-ku Tokyo 100-0004

JAPON

Date of mailing (day/month/year)

10 September 1999 (10.09.99)

Applicant's or agent's file reference

YCT-395

IMPORTANT INFORMATION

International application No. PCT/JP99/01080

International filing date (day/month/year)

05 March 1999 (05.03.99)

Priority date (day/month/year) 06 March 1998 (06.03.98)

Applicant

CHUGAI SEIYAKU KABUSHIKI KAISHA et al

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

AP :GH,GM,KE,LS,MW,SD,SL,SZ,UG,ZW

EP:AT,BE,CH,CY,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE

National :AU,BG,BR,CA,CN,CZ,DE,GB,IL,JP,KR,MN,NO,NZ,PL,RO,RU,SE,SK,US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

EA:AM,AZ,BY,KG,KZ,MD,RU,TJ,TM

OA:BF,BJ,CF,CG,CI,CM,GA,GN,GW,ML,MR,NE,SN,TD,TG

National :AL,AM,AT,AZ,BA,BB,BY,CH,CU,DK,EE,ES,FI,GD,GE,GH,GM,HR,HU,ID,IN,

IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MW,MX,PT,SD,SG,SI,SL,TJ,TM,TR,

TT,UA,UG,UZ,VN,YU,ZW

3. The applicant is reminded that he must enter the "national phase" before the expiration of 30 months from the priority date before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing a translation of any translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed until 31 months from the priority date for all States designated for the purposes of obtaining a European patent.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer:

J. Zahra

Telephone No. (41-22) 338.83.38

Facsimile No. (41-22) 740.14.35

PCT

REQUEST

For receiving Office	use only
International Application No.	
International Filing Date	5/3/99
Name of receiving Office and "PCT Into	ernational Application"

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.	Name of receiving Office	and "PCT International Application"			
	Applicant's or agent's file (if desired) (12 characters mo	V('''= 1U')			
Box No. I TITLE OF INVENTION					
PROTEIN-FREE FORMULATIONS					
Box No. II APPLICANT					
Name and address: (Family name followed by given name; for a designation. The address must include postal code and name of co address indicated in this Box is the applicant's State (that is, country of residence is indicated below.) CHUGAI SEIYAKU KABUSHIKI KAISHA	y) of residence if no State	This person is also inventor. Telephone No.			
5-1, Ukima 5-chome, Kita-ku,					
Tokyo 115-8543 Japan	•	Facsimile No.			
10ky0 115-0545 bapan	•	Teleprinter No.			
State (that is, country) of nationality: Japan	State (that is, country) of Japan	residence:			
This person is applicant all designated for the purposes of: States V all designated the United States		United States America only the States indicated in the Supplemental Box			
Box No. III FURTHER APPLICANT(S) AND/OR (FURT	HER) INVENTOR(S)				
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) SUMIDA, Shuji					
c/o Chugai Seiyaku Kabushiki K 41-8, Takada 3-chome, Toshima-		inventor only (If this check-box			
Tokyo 171-8545 Japan		is marked, do not fill in below.)			
State (that is, country) of nationality: Japan	State (that is, country) of Japan	residence:			
This person is applicant all designated for the purposes of:		e United States			
V Further applicants and/or (further) inventors are indicated	on a continuation sheet.				
Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE					
The person identified below is hereby/has been appointed to act of the applicant(s) before the competent International Authoritie	on behalf v a	gent common representative			
Name and address: (Family name followed by given name; for designation. The address must include postal a SHAMOTO, Ichio, (8970) Patent A	tode and name of continy.)	Telephone No. (03) 3270-6641			
YUASA AND HARA, Section 206, New		Facsimile No. (03) 3246-0233			
Bldg., 2-1, Ohtemachi 2-chome, (Chiyoda-ku,				
Tokyo 100-0004 Japan		Teleprinter No			
Address for correspondence: Mark this check-box where space above is used instead to indicate a special address to	no agent or common repres	entative is/has been appointed and the ald be sent.			

		2
heet	Nο	_

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)				
If none of the following sub-boxes is used, this sheet should not be	included in the request.			
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) This person is: applicant only				
SATO, Yasushi	V applicant and inventor			
c/o Chugai Seiyaku Kabushiki Kaisha				
41-8, Takada 3-chome, Toshima-ku,	inventor only (If this check-box is marked, do not fill in below.)			
Tokyo 171-8545 Japan				
State (that is, country) of nationality: Japan State (that is, country) of Japan Japan	of residence:			
	he United States of America only the States indicated in the Supplemental Box			
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)	This person is:			
	applicant and inventor			
	inventor only (If this check-box			
	is marked, do not fill in below.)			
State (that is, country) of nationality: State (that is, country)	or residence.			
	he United States in the States indicated in the Supplemental Box			
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)	This person is:			
	applicant and inventor			
	inventor only (If this check-box is marked, do not fill in below.)			
State (that is, country) of nationality: State (that is, country)	of residence:			
State (maris, columy) of nationality.				
	the United States of America only the States indicated in the Supplemental Box			
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)	This person is: applicant only			
	applicant and inventor			
	inventor only (If this check-box is marked, do not fill in below.)			
State (that is, country) of nationality: State (that is, country)	of residence:			
This person is applicant all designated all designated States except the United States of America	the United States of America only the States indicated in the Supplemental Box			
Further applicants and/or (further) inventors are indicated on another continuation sheet.				

Box N	o.V	DESIGNATION OF STATES				
The fo	The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):					
Region	nal Pa	atent			·	
Ø	AP	ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, LIC Hoanda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT				
V	EA	Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Furasian Patent Convention and of the PCT				
V	EP	European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT				
⊻	OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)					
Nation	al Pote	nt (if other kind of protection or treatment desired, specify	on dot	ted line	າ):	
		United Arab Emirates	_			
	AE AT	Albania	ᅜ		Liberia	
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V		Armenia	<u> </u>		Lithuania	
		Austria	♡		Luxembourg	
		Australia			Latvia	
团		Azerbaijan	团		Republic of Moldova	
⊻		Bosnia and Herzegovina	团	MG	Madagascar	
▽		Barbados	∇	MK	The former Yugoslav Republic of Macedonia	
☑		Bulgaria				
☑	BR	Brazil	∇		Mongolia	
	BY	Belarus	$\overline{\square}$		Malawi	
☑		Canada	∇	MX	Mexico	
☑		and Ll Switzerland and Liechtenstein	V	NO	Norway	
₩		China	∇	NZ	New Zealand	
		Cuba	V		Poland	
	CZ			PT		
	DE		∇		Romania	
	-	Denmark	☑		Russian Federation	
		Estonia	<u>⊠</u>	SD	Sudan	
	ES	Spain	<u>₩</u>	SE	Sweden	
	ES Fl	Finland	<u>₩</u>	SG	Singapore	
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	lD	Indonesia	团		Ukraine	
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♡	IN	India	∇	US		
☑		Iceland				
	JP	Japan	∇		Uzbekistan	
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٦ ا	, .	Democratic reopie's Republic of Research		ZW		
	y/m	Republic of Korea	Ch	eck-b	oves reserved for designating States which have	
			bec	come r	party to the PCT after issuance of this sheet:	
		Kazakhstan		_	······································	
		Saint Lucia	닏			
V	LK	Sri Lanka	<u> </u>		handle and least also makes under Rule 4 9(b) all other	
Proc	autio	nary Designation Statement: In addition to the desig	nation	is mad	c above, the applicant also makes under Kule 4.9(b) all other	

designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Supplemental Box If the Supplemental Box is not used, this sheet should not be included in the request.

- 1. If, in any of the Boxes, the space is insufficient to furnish all the information: in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:
 - (i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;
- (ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Conti
- (iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all design ated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;
- (iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;
- (v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;
- (vi) if, in Box No. 17, there are more than three earlier applications whose priority is claimed: in such case, write "Continuation of Box No. 17" and indicate for each additional earlier application the same type of information as required in Box No. 17;
- (vii) if, in Box No. 17, the earlier application is an ARIPO application: in such case, write "Continuation of Box No. 17", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed.
- 2. If, with regard to the precautionary designation statement contained in Box No. 1', the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.
- 3. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty: in such case, write "Statement concerning non-prejudicial disclosures or exceptions to lack of novelty" and furnish that statement below.

"Continuation of Box No. IV"

The same address as Box IV

IMAI, Shosuke, (7112) Patent Attorney
MASUI, Chuji, (7669) Patent Attorney
KURITA, Tadahiko, (7523) Patent Attorney
KOBAYASHI, Yasushi, (7527) Patent Attorney
EJIRI, Hiroko, (9163) Patent Attorney

Sheet No. ...5....

Box No. VI PRIORITY CLAIM Further priority claims are indicated in the Supplemental Box.					
Filing date	Number		Where earlier applica		
of earlier application (day/month/year)	of earlier application	national applie	1000	international application: receiving Office	
item (1) 6/3/1998	54799/19	98 Japa:	n.		
item (2)		·			
				· · · · · · · · · · · · · · · · · · ·	
item (3)					
The receiving Office is recoff the earlier application (spurposes of the present in			tional Bureau a certified copy with the Office which for the e) identified above as item(s)	(1)	
	40100		e in the Supplemental Box at least on on was filed (Rule 4.10(b)(ii)). See i	one country party to the Paris Supplemental Box.	
	NAL SEARCHING	AUTHORITY			
Choice of International Search if two or more International Second competent to carry out the second competent to carry	arching Authorities are ational search, indicate	Request to use resusearch has been carried Date (day/month/year)	Its of earlier search; reference if out by or requested from the Intern Number	e to that search (if an earlier national Searching Authority): Country (or regional Office)	
the Authority chosen, the two-letter ISA / JP	coue may be used).	Date (uny/months/eur)	2		
Box No. VIII CHECK LIST	T; LANGUAGE OF	FILING			
This international application of the following number of shee	contains This intern	ational application is a	eccompanied by the item(s) man	rked below:	
request :	E 1. [V] 1ee	calculation sheet			
description (excluding	2. ▼ sepa	arate signed power of			
sequence listing part)	-		attorney, reference number, if a	illy.	
claims : 2 4. statement explaining lack of signature					
abstract :			tified in Box No. VI as item(s):		
drawings :			l application into (language):	a 1 1	
sequence listing part of description	· —		erning deposited microorganism		
	8. 🔲 nuc	leotide and/or amino a	cid sequence listing in compute	r readable form	
Total number of sheets:	22 9. 🔯 oth		st for transmittal of ty document	·	
Figure of the drawings which should accompany the abstract		Language of filing international applic	of the Japanese		
Box No. IX SIGNATURE	OF APPLICANT O	R AGENT			
Next to each signature, indicate the n	ame of the person signing a	nd the capacity in which th	e person signs (if such capacity is not o	bvious from reading the regilest).	
SНАМОТО. ТО	hio, (8970)	Patent Att	ornev		
IMAI, Shosu	ke, (7112)	Patent Atto	rney		
MASUI, Chuj	i, (7669) P	atent Attor	ney		
KURITA, Tad	lahiko, (752	3) Patent A	ttorney		
KOBAYASHI, Yasushi, (7527) Patent Attorney					
EJIRI, Hiroko, (9163) Patent Attorney					
				<u> </u>	
For receiving Office use only 2. Drawings:					
international application:					
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:					
4. Date of timely receipt of the required corrections under PCT Article 11(2):					
5. International Searching Authority ISA / JP 6. Transmittal of search copy delayed until search fee is paid.					
	Fo	or International Bureau	use only		
Date of receipt of the record by the International Bureau:			•		